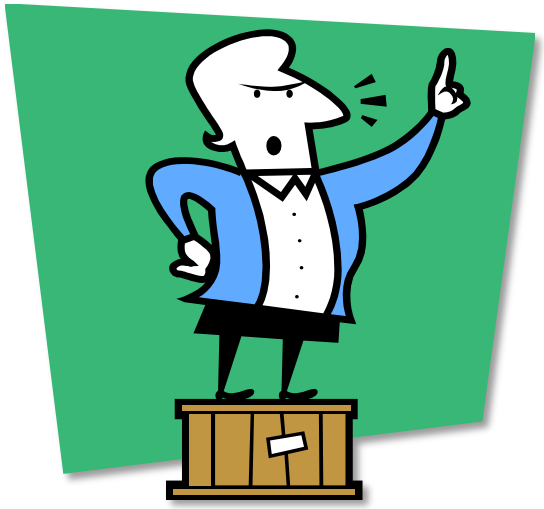
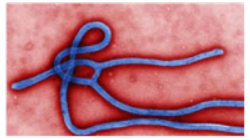
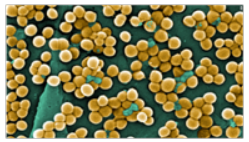
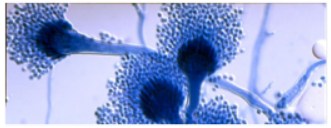
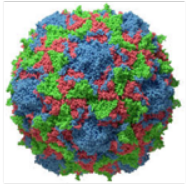
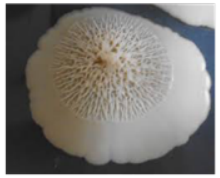
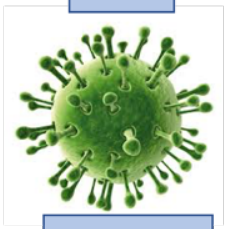
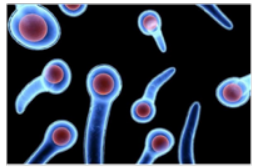
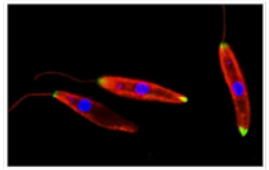
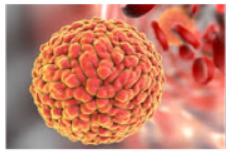
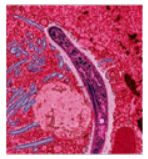
Thema der Vorlesung

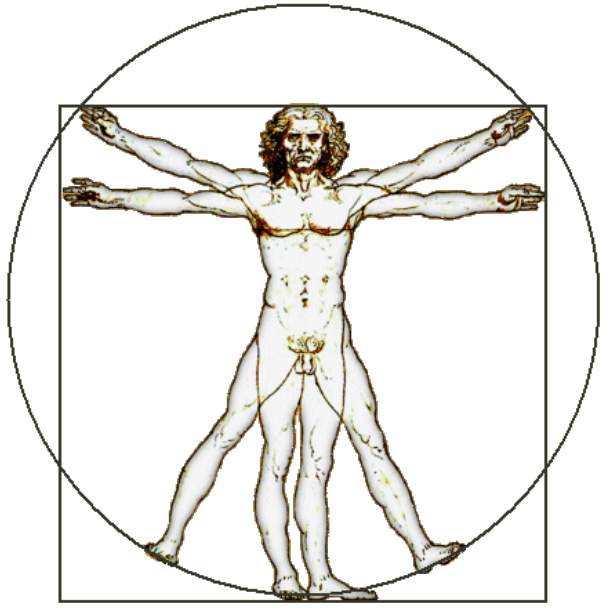


Biofilme am/im Menschen

- Humanes Mikrobiom
- Mikrobielle Infektion

Viruses/Phages	Bacteria	‚small' Eukarya
		
Ebola	*Staph. aureus (MRSA)*	*Aspergillus fumigatus*
		
Polio	*Vibrio cholerae*	*Candida albicans*
		
Influenza	*Clostridium tetani*	*Leishmania tropica*
		
Zika	*E. coli EHEC*	*Plasmodium falciparum*

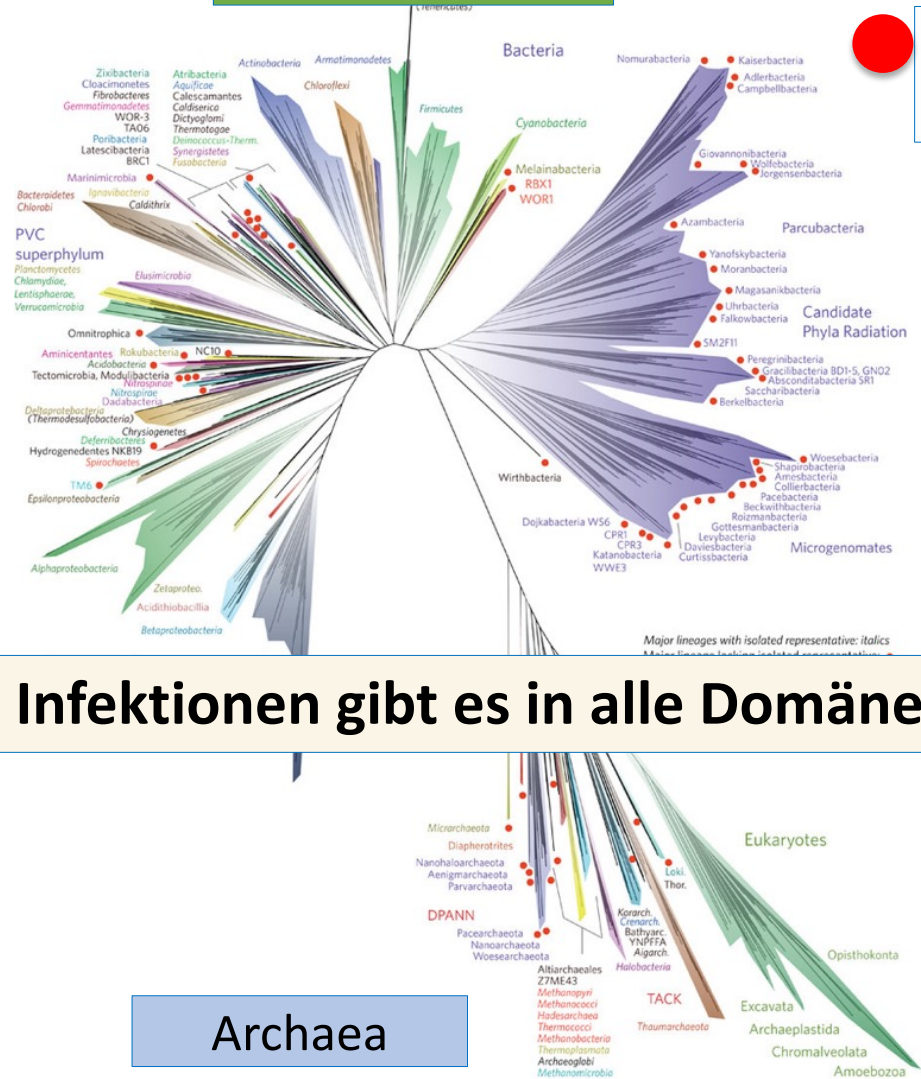
Infektion/Entzündung/
Interaktion



Abwehr/Immunität/
Resistenz

Viruses/Bacteriophages 10^{31} particles
Bacteria/Archaea 10^{30} cells on earth
Whitmann et al., 2001 PNAS,
C. Magnabosco, Nature Geoscience, 2018,

Bacteria

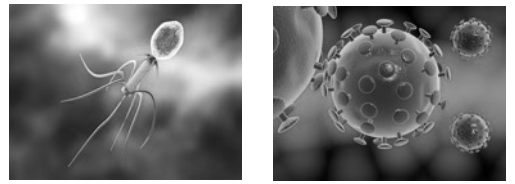


Nature Microbiology, 2016 Banfield et al.

No cultivated isolate available

Infektionen gibt es in alle Domänen des Lebens!

B A E



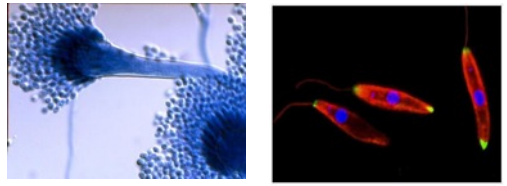
Bacteriophage/Virus

B E

Bacteria/Archaea

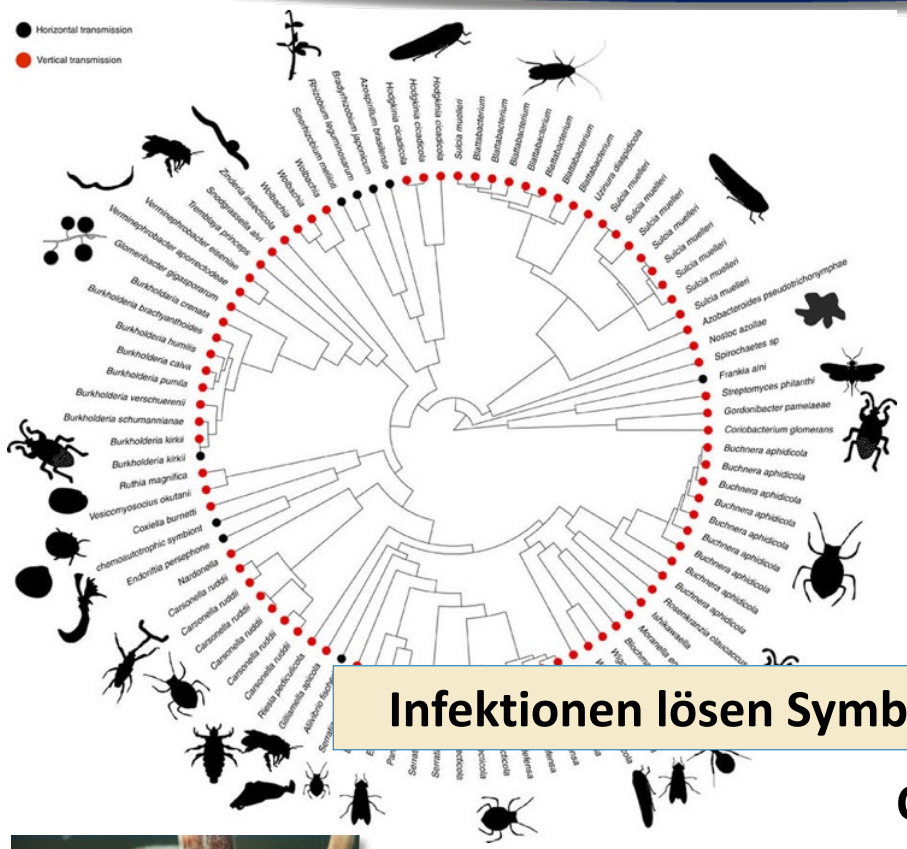
Paez-Espino, 2016, NAR

E

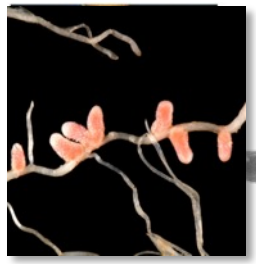


Fungi/Small Eukaryotes

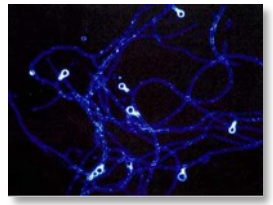
Fischer et al., *Nature Communications* **8**, 2017



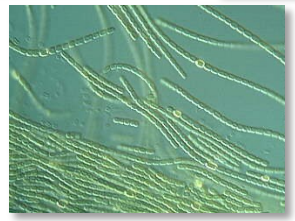
Rhizobium x Legume



Frankia x Alnus



Cyanobacteria x Azolla



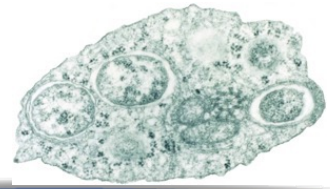
Images from Microbe Wiki, ASM & JGI

Infektionen lösen Symbiosen aus mit Folgen für die globalen N & C Kreisläufe

Cand. Endoriftia persephone x Tubeworms (Riftia)

Mycorrhiza x plants

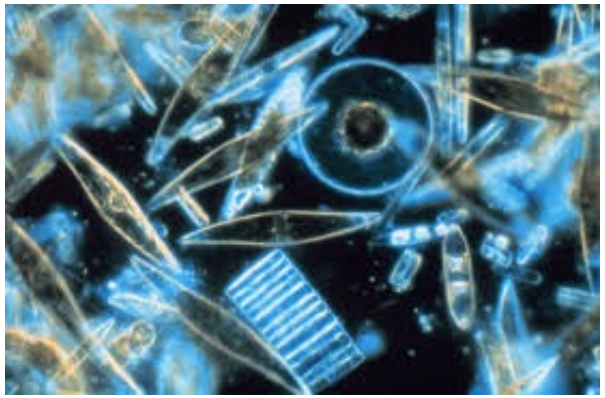
Wollbachia sp. x Insects



Corral Reefs

Macro- / Microalgae

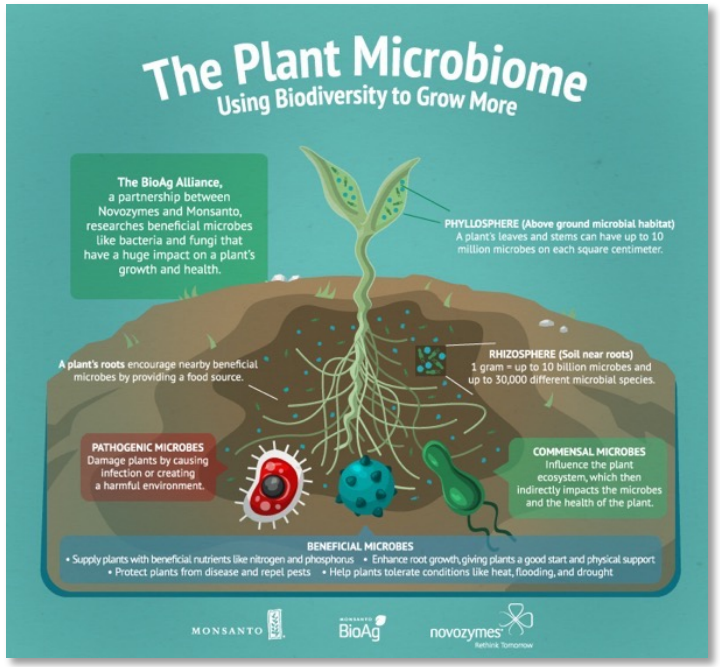
Plancton



Infections affect climate and global nutrient cycles !

Infections/Microbes modify global ecosystems

Infections are drives for biodiversity & evolution


The Plant Microbiome
Using Biodiversity to Grow More
The BioAg Alliance, a partnership between Novozymes and Monsanto, researches beneficial microbes like bacteria and fungi that have a huge impact on a plant's growth and health.
PHYLLOSPHERE (Above ground microbial habitat)
A plant's leaves and stems can have up to 10 million microbes on each square centimeter.
A plant's roots encourage nearby beneficial microbes by providing a food source.
RHIZOSPHERE (Soil near roots)
1 gram = up to 10 billion microbes and up to 30,000 different microbial species.
PATHOGENIC MICROBES
Damage plants by causing infection or creating a harmful environment.
COMMENSAL MICROBES
Influence the plant ecosystem, which then indirectly impacts the microbes and the health of the plant.
BENEFICIAL MICROBES
• Supply plants with beneficial nutrients like nitrogen and phosphorus • Enhance root growth,giving plants a good start and physical support
• Protect plants from disease and repel pests • Help plants tolerate conditions like heat, flooding, and drought
MONSANTO
BioAg
novozymes

Microbes have impact on agriculture, food & forestry!

Major pathogens

Fungi:

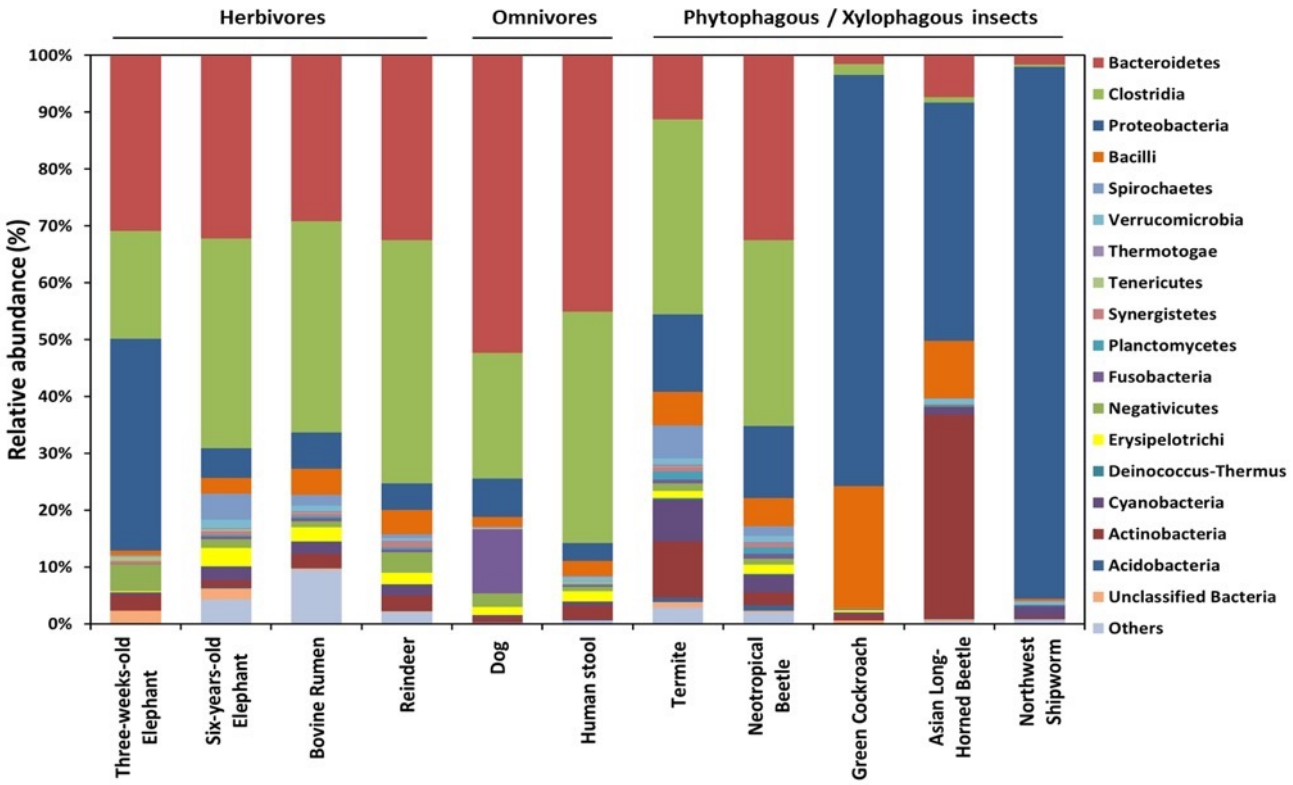
(1) *Magnaporthe oryzae*
(2) *Botrytis cinerea*
(3) *Puccinia* spp.
(**4**) ***Fusarium graminearum***
(5) *Fusarium oxysporum*
…

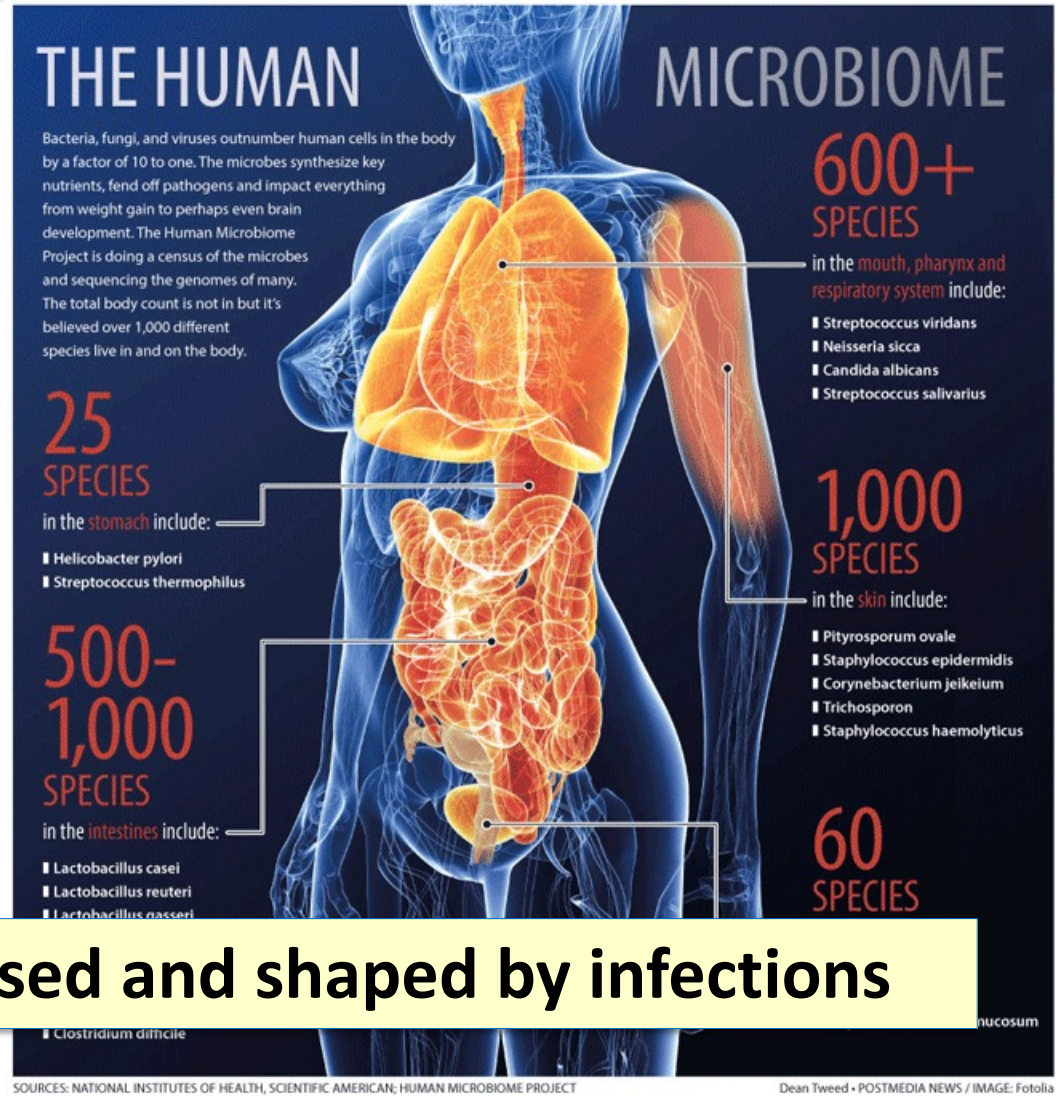
Bacteria:

(1) Pseudomonas syringae
(2) Burkholderia glumae
(3) Erwinia caratovora & amylovorans
…

Viruses:

(1) Tobacco mosaic virus
(2) Tomato spotted wilt virus
(3) Potato virus Y
…




THE HUMAN MICROBIOME
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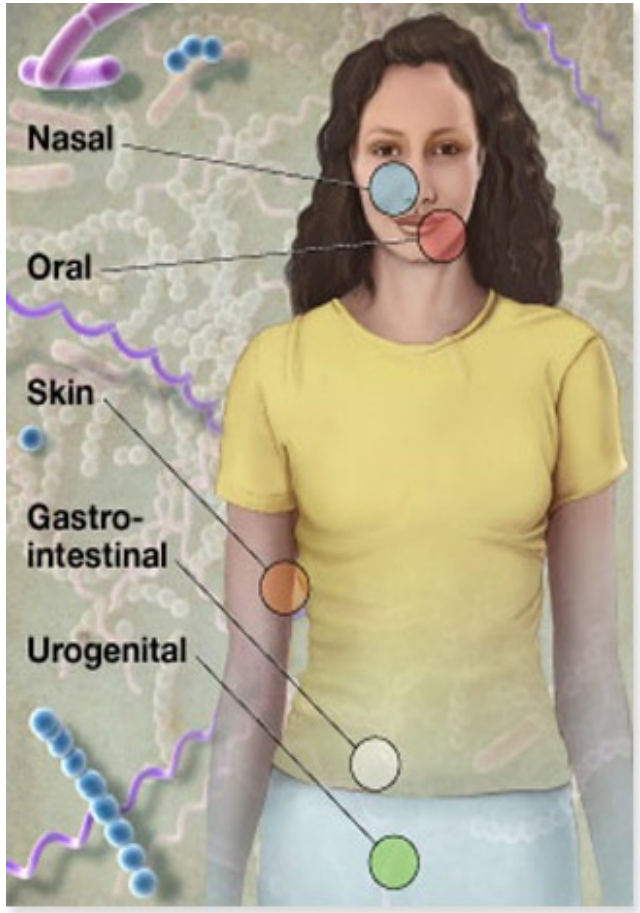
Lactobacillus reuteri
60 SPECIES
Clostridium difficile
SOURCES: NATIONAL INSTITUTES OF HEALTH, SCIENTIFIC AMERICAN; HUMAN MICROBIOME PROJECT
Dean Tweed • POSTMEDIA NEWS / IMAGE: Fotolia

Stable microbiomes are in part caused and shaped by infections

Wozu sind Bakterien im Darm überhaupt gut und worauf nehmen sie Einfluss ?

- Vitaminversorgung
- Fettsucht
- Immunabwehr und Stimulation des Immunsystems
- Metabolisierung von Antibiotika und Xenobiotika, etc...

- 10^{12} Zellen pro Gramm Faeces, ca. tausend Spezies pro Individuum
- hoher Gradient vom Jejenum bis zum duodenum
- 5 Mio Gene bei 10^{14} Zellen
- 80% nicht kultivierte Mikroorganismen
- 100-1.000-fach mehr anaerobe als aerobe oder fakultative

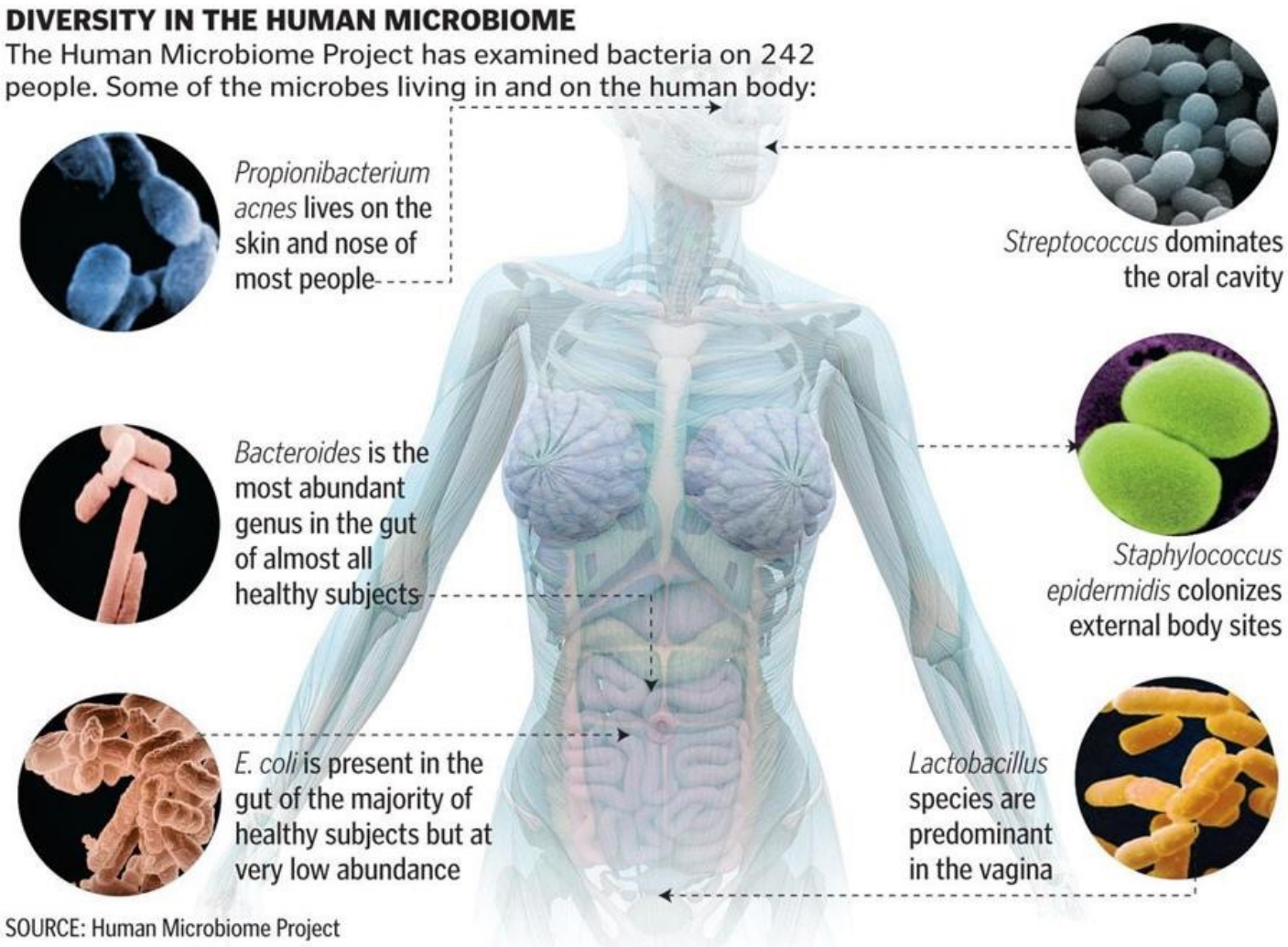


Erwachsene: *Bacteroidetes*, *Ruminococcus* und *Prevotella*, *Eubacterium*, Actinobacteria, Proteobacteria

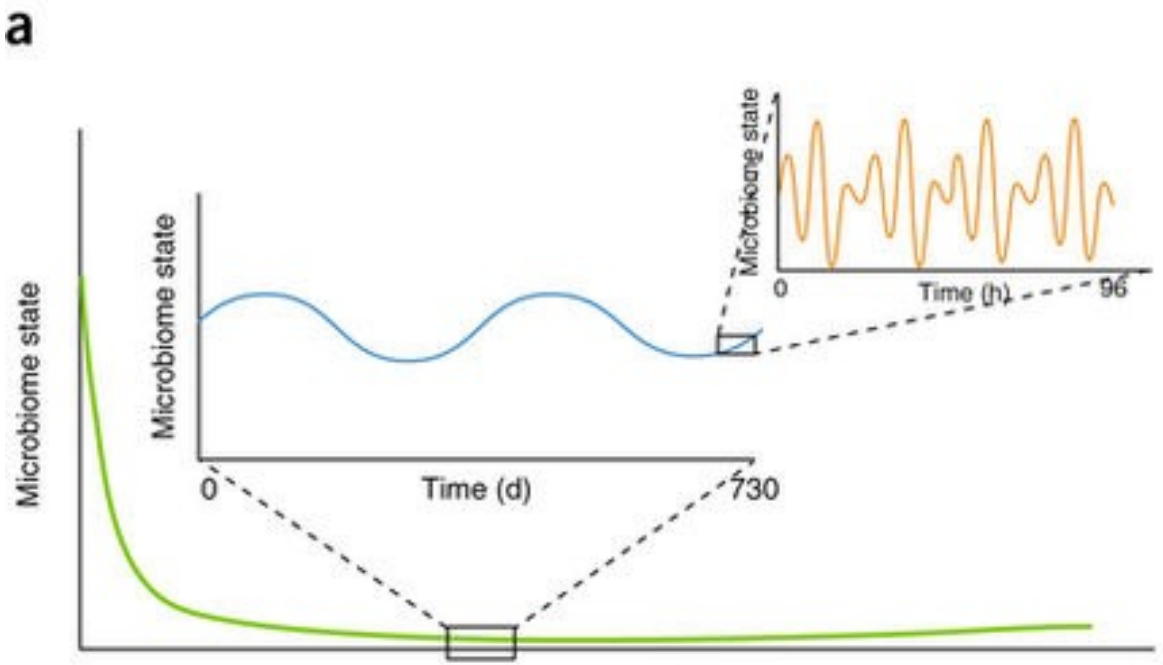
Neugeborene: *Staphylococcus*, *Streptococcus*, *Bifidobacterium* and *Enterobacteria*

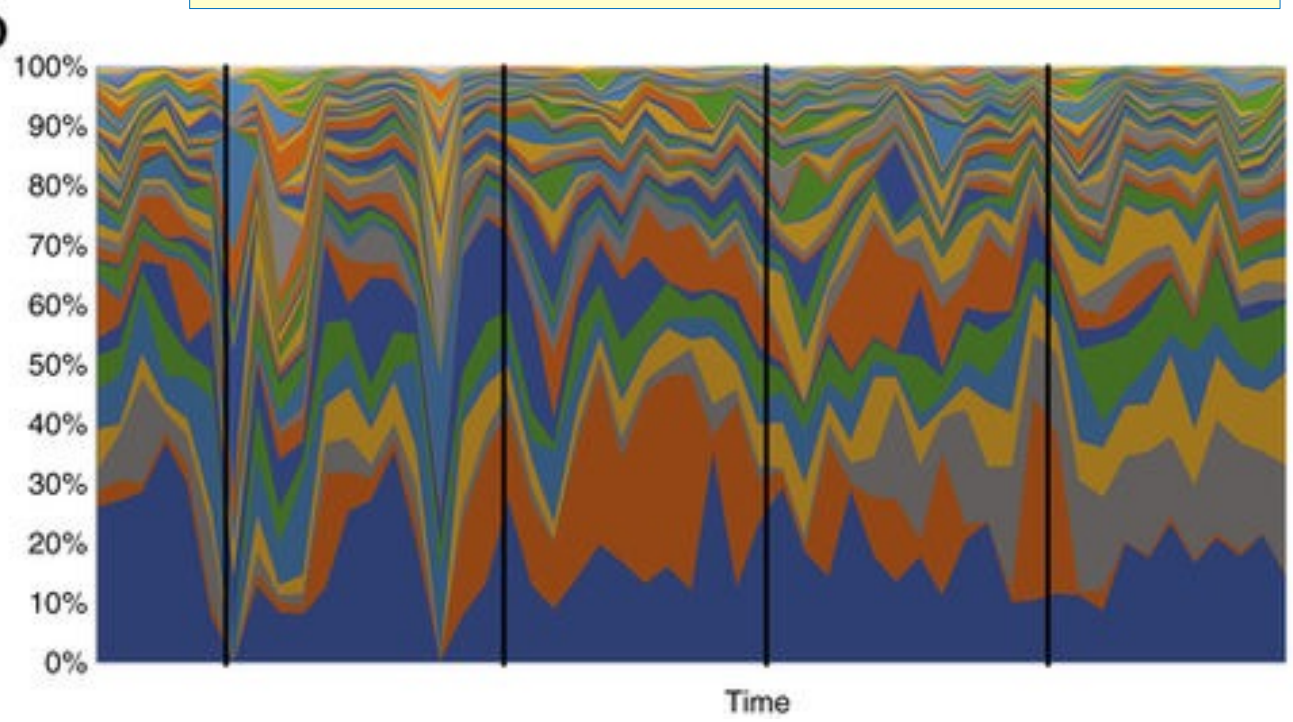
Beim Menschen gefundene Keimzahlen

• Kopfhaut	• $1{,}5 \times 10^6$ / cm^2
• Achselhöhle	• $2{,}4 \times 10^6$ / cm^2
• Unterarm	• $1{,}0 – 4{,}5 \times 10^3$ / cm^2
• Rücken	• $3{,}1 \times 10^2$ / cm^2
• Stirn	• $2{,}0 \times 10^5$ / cm^2
• Nasensekret	• $10^6 – 10^7$ / g
• Cerumen des Gehörganges	• bis 10^8 / g
• Speichel	• $10^7 – 10^8$ / ml
• Stuhl	• 10^{11} / g
• (*E. coli* im Stuhl	• $10^7 – 10^8$ / g)


DIVERSITY IN THE HUMAN MICROBIOME
The Human Microbiome Project has examined bacteria on 242 people. Some of the microbes living in and on the human body:
Propionibacterium acnes lives on the skin and nose of most people
Streptococcus dominates the oral cavity
Bacteroides is the most abundant genus in the gut of almost all healthy subjects
Staphylococcus epidermidis colonizes external body sites
E. coli is present in the gut of the majority of healthy subjects but at very low abundance
Lactobacillus species are predominant in the vagina
SOURCE: Human Microbiome Project

Das humane Mikrobiom ist sehr variabel





1) über die Zeit in der Gesamtzahl und

2) in der Spezieszusammensetzung!

Gilbert et al., 2018, Nature Review
https://www.nature.com/articles/nm.4517#f2

- **Verhältnis humane Körperzellen zu Mikobiom:**
  verschiedene, aber doch ähnliche Aussagen
- **1,3 mal mehr Bakterien als eigene Zellen; aber auch deutlich mehr Phagen und Pilzzellen als humane Zellen**
- **Ca. 1,2-1,5 kg**

  Humane Zellen ca.: 5 - 724 × 10^{12}

  Bakterielle und Archaeelle Zellen ca. : 30 - 400 × 10^{12}

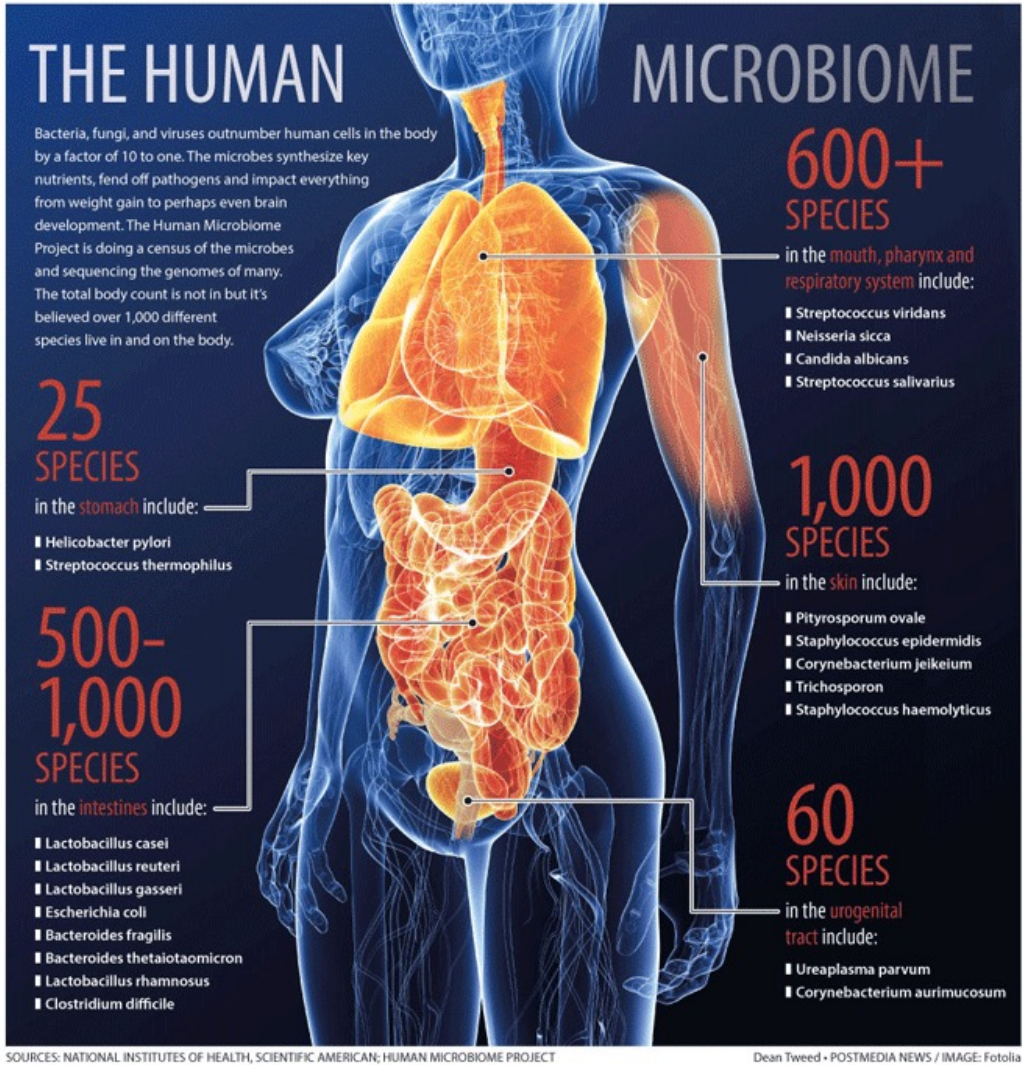
  Rosner, J.L. Ten times more microbial cells than body cells in humans? *Microbe* 9, 47 (2014)

  Verhältnis 10:1 humane Zellen/Bakterien

  Luckey, T.D. Introduction to intestinal microecology. *Am. J. Clin. Nutr.* 25, 1292–1294 (1972)
- **Achtung Pilze und und andere niedrige Eukaryonten sowie Viren sind nicht berücksichtigt**

- **1.000 Spezies im Intestinaltrakt:**
- Jede Spezies ca. 2,000 Genes:
  Ergo ca. 2.000. 000 Gene, das sind
- 100 x mehr Gene, als das Humane Genom mit ca. 20.000 Genen!

Diese Zahlen korrelieren sehr gut mit den Zahlen des Microbial gene catalogs obtained by MetaHIT und Human Microbiome Project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Streptococcus salivarius
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Corynebacterium jeikeium
Trichosporon
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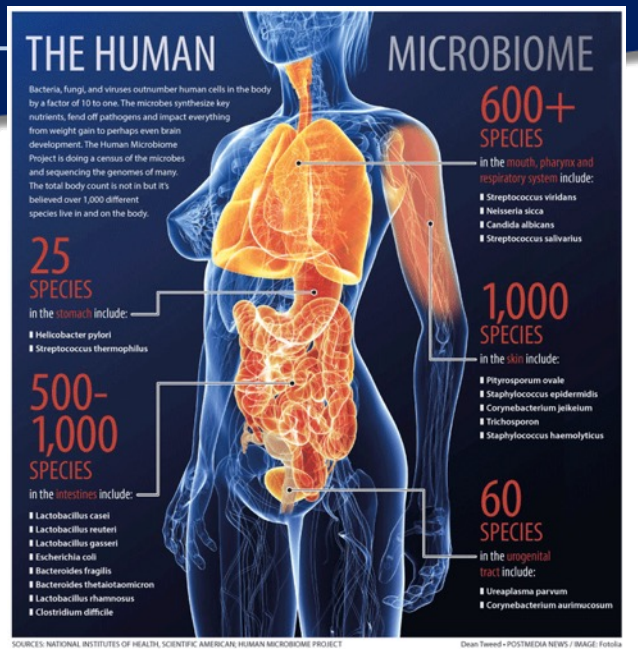
Lactobacillus reuteri
Lactobacillus gasseri
Escherichia coli
Bacteroides fragilis
Bacteroides thetaiotaomicron
Lactobacillus rhamnosus
Clostridium difficile
60 SPECIES in the urogenital tract include:
Ureaplasma parvum
Corynebacterium aurimucosum
SOURCES: NATIONAL INSTITUTES OF HEALTH, SCIENTIFIC AMERICAN; HUMAN MICROBIOME PROJECT
Dean Tweed • POSTMEDIA NEWS / IMAGE: Fotolia

Essential and Beneficial Functions of the Microbiome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Dean Tweed • POSTMEDIA NEWS / IMAGE: Fotolia

- Vitamin supply with essential vitamins (mostly B-vitamins)

- Stimulation of the immune system

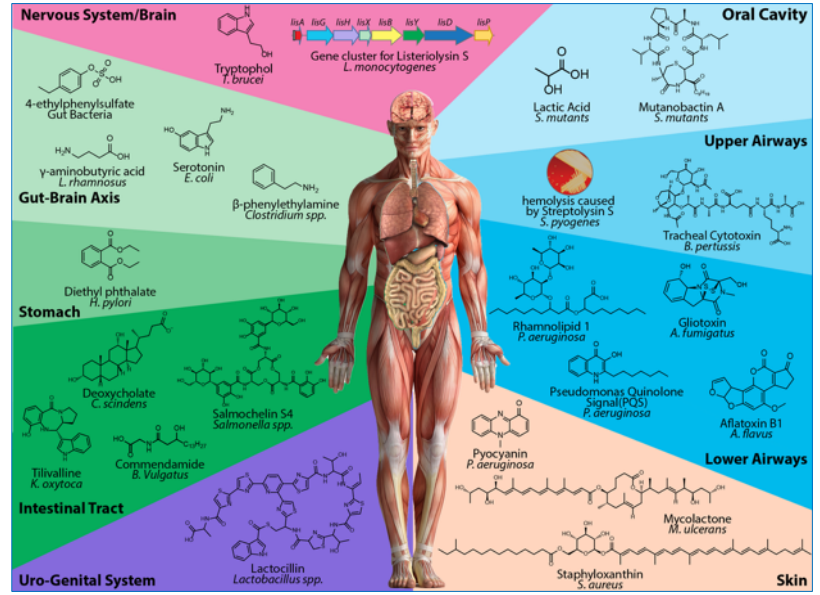
- Continous Pathogen defense
  (competition for space, pH, antimicrobial peptides, antibiotics)

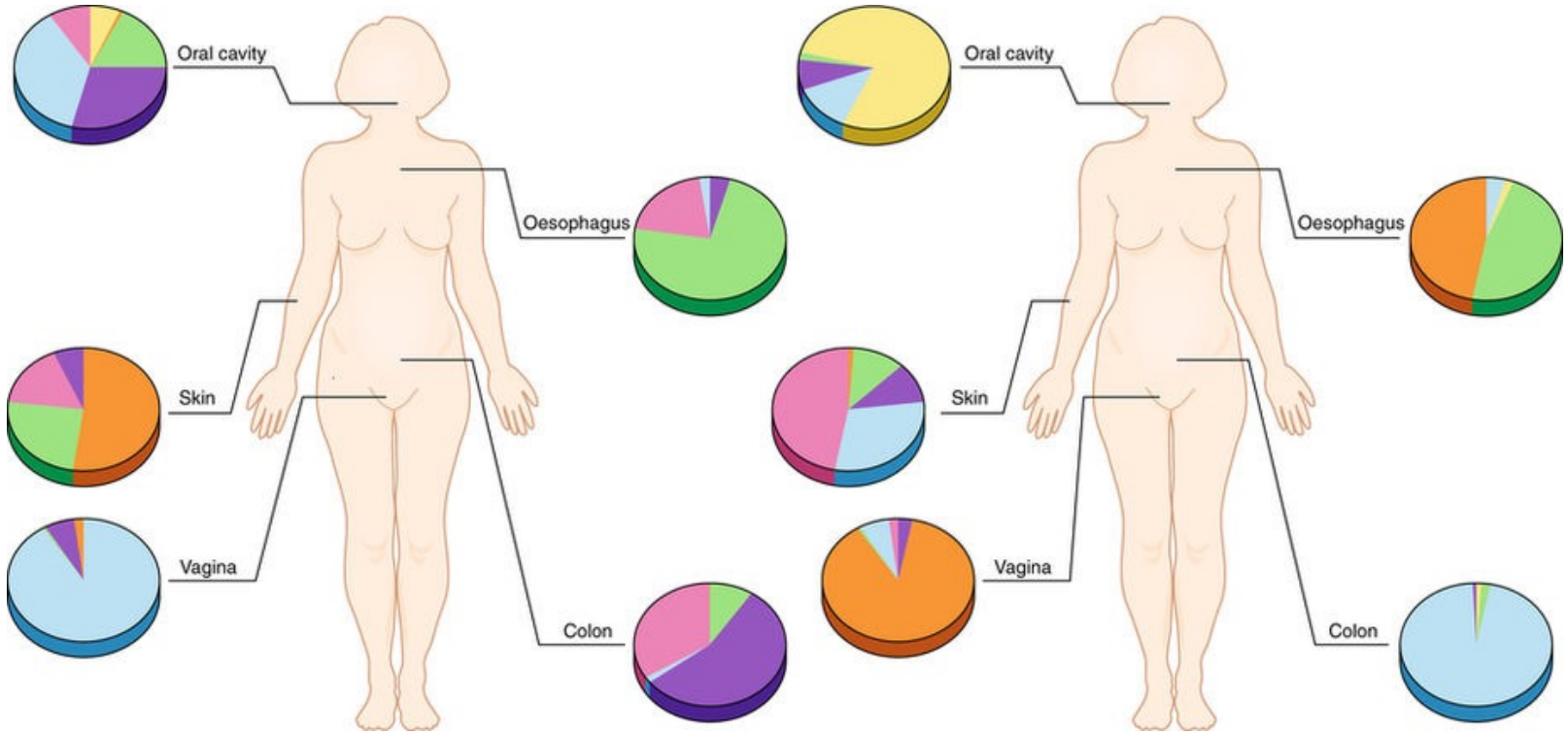
- Supply of metabolites other than vitamins

- Digestion of food and nutrients (production exoenzymes!)

- Supports uptake of nutrients

- Detoxification/degradadtion/ modification of xenobiotics/metabolites

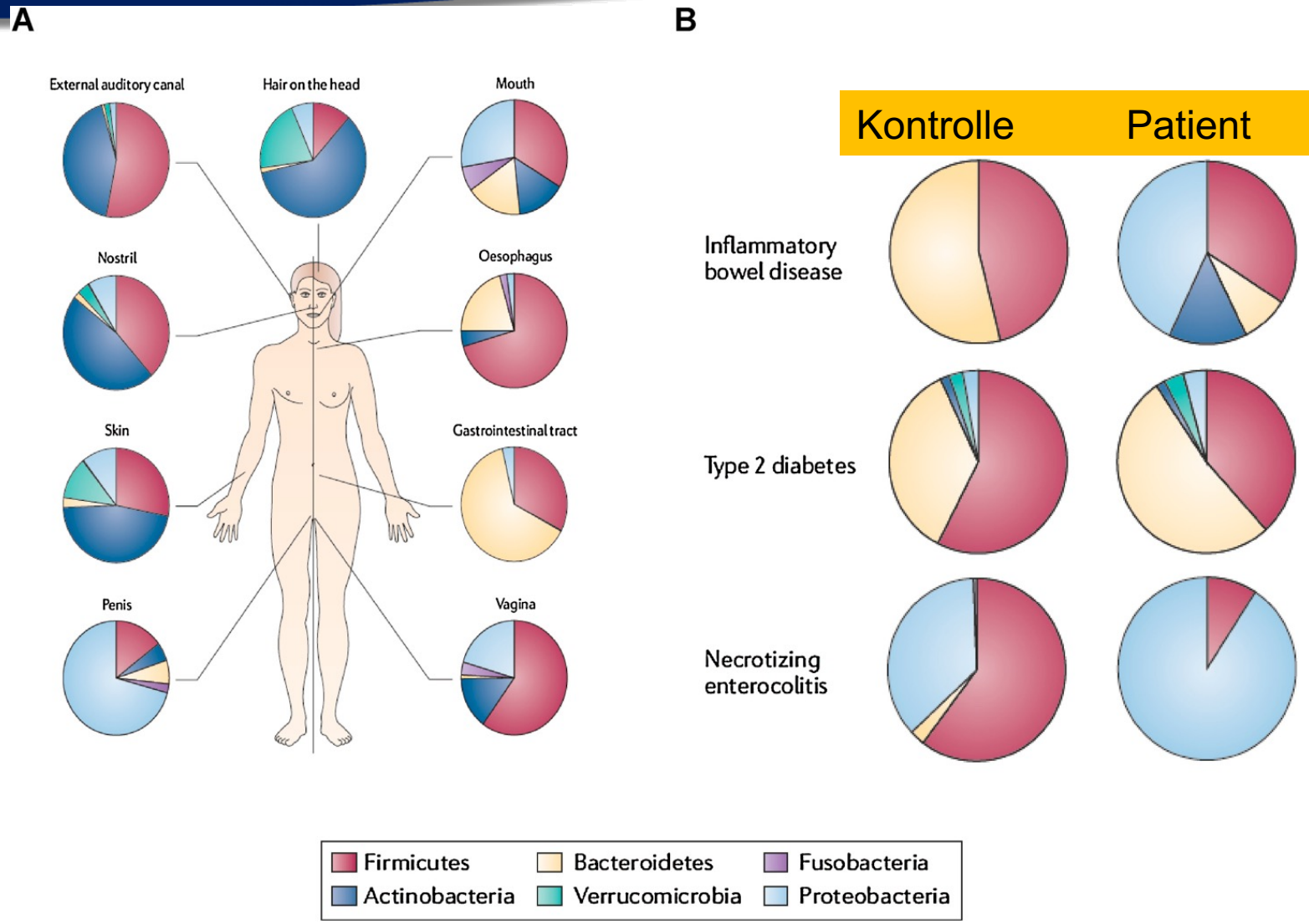




- Each individual has its own microbiome composition
- Understanding the relevance of the differing microbiota between individuals is confounded by the uniqueness of an individual's microbiome
- Composition is somewhat similar if people live in the same household....

Gilbert et al., 2018, Nature Reviews
https://www.nature.com/articles/nm.4517#f2

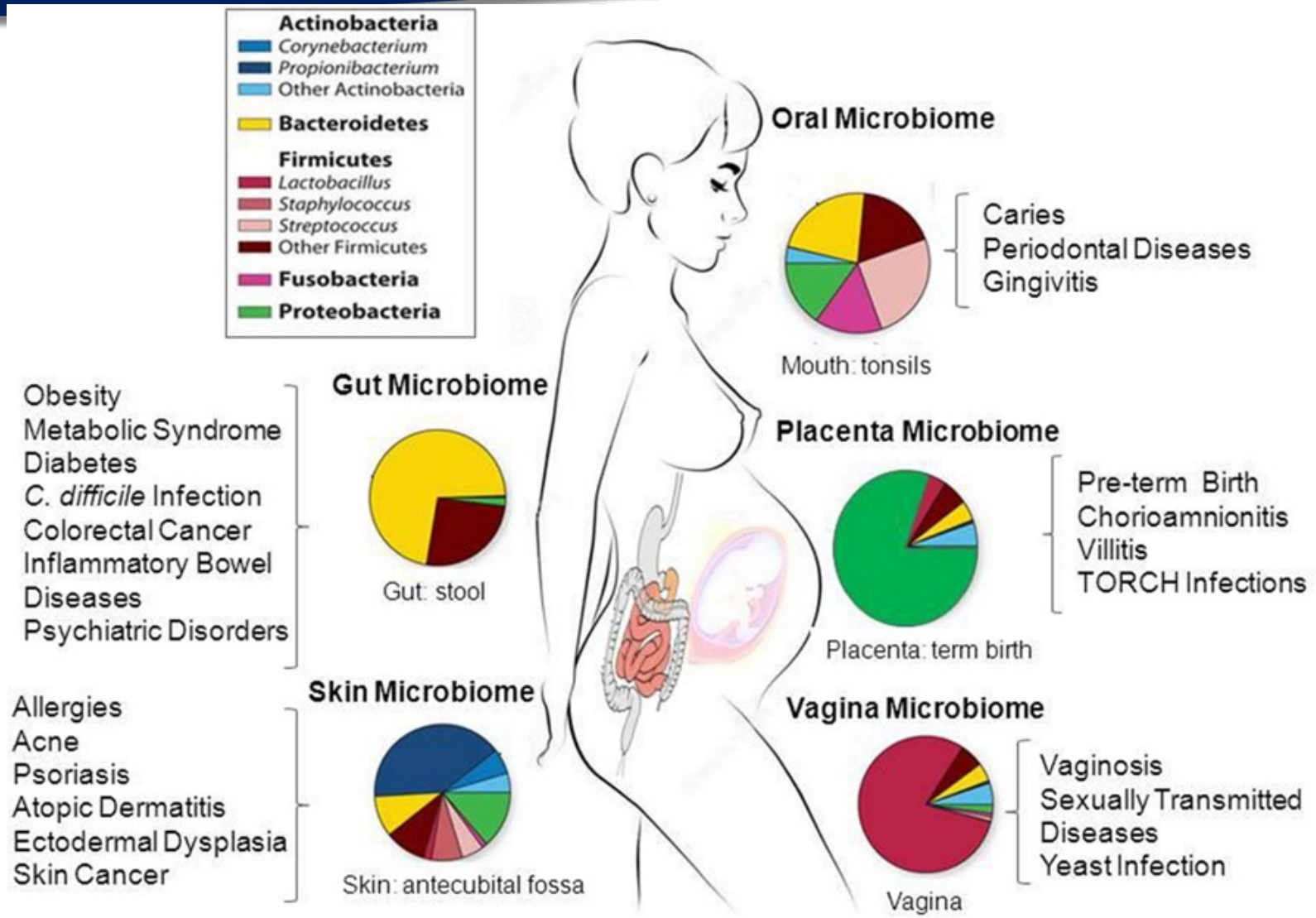
Einige Krankheiten, die mit einem veränderten Mikrobiom in Zusammenhang (!) stehen



Blum, The Human Microbiome, 2017 Advances in Medical Sciences

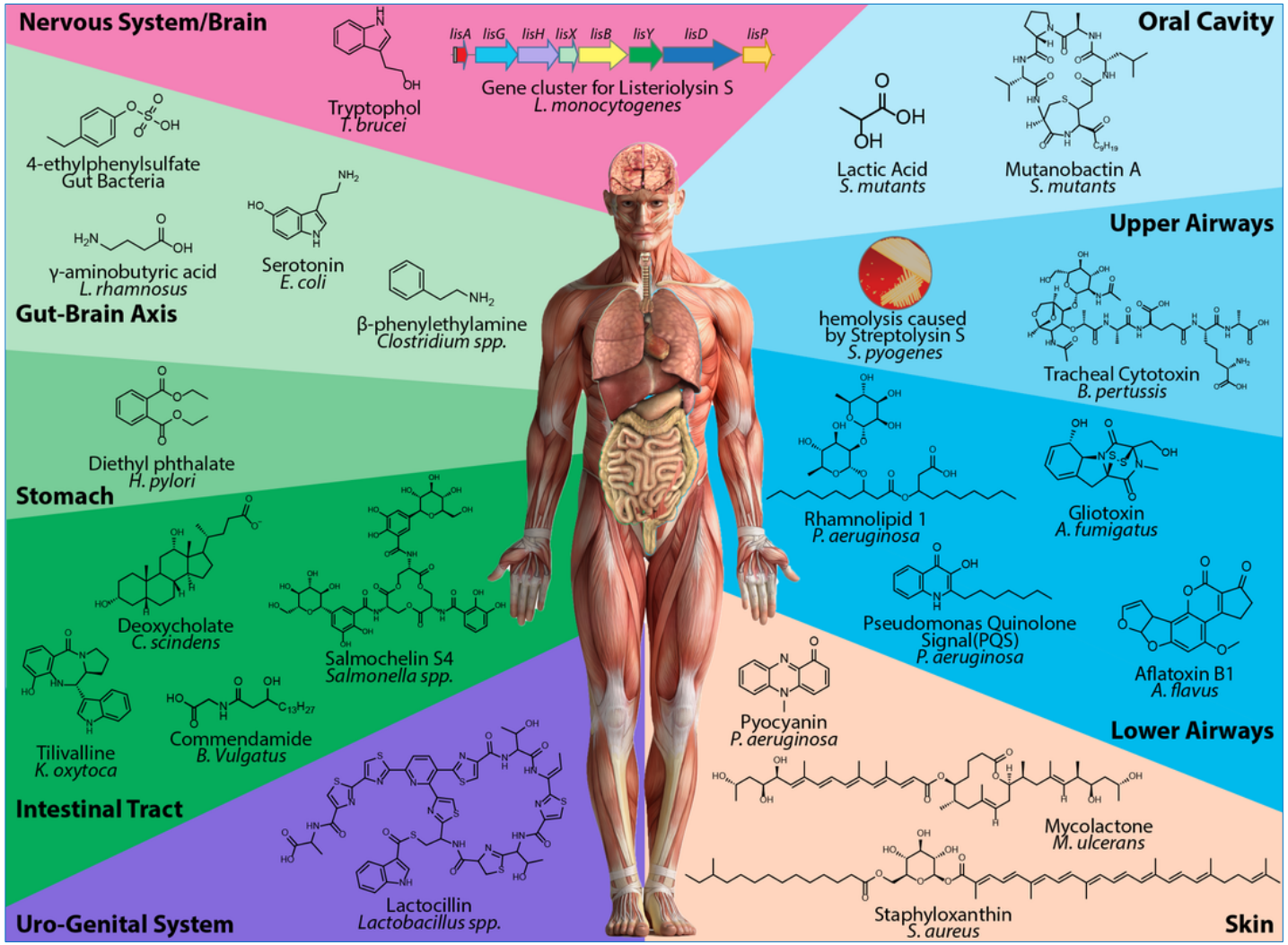
A. Spor, O. Koren, R. Ley Nat Rev Microbiol, 9 (2011), pp. 279-290

Krankheiten assoziiert (!), aber nicht unbedingt hervorgerufen durch ein verändertes humanes Mikrobiom



A. Spor, O. Koren, R. Ley Nat Rev Microbiol, 9 (2011), pp. 279-290

Bakterienmetabolite nehmen direkten Einfluss auf den humanen Stoffwechsel!



Garg et al, Natural Products report 2016 .
http://pubs.rsc.org/en/content/articlelanding/2017/np/c6np00063k#!divAbstract

Wichtig: Die Nahrung verändert und selektioniert die mikrobielle Flora im Darm

Faktoren, die diese in der Zusammensetzung beeinflussen:

Antibiotika, Fruktosesirup, Chlor, Pharmazeutische Wirkstoffe, Weichmacher,
High carbohydrate /vs. low carbohydrate Food
“Fibers”, “vegetabels” und…….viele andere

Achtung: fettleibige Mäuse haben einen höheren Titer an ‘Firmicutes’ im Vgl. zu normalgewichtigen. Dort sind die ‘Bacteriodetes’ überwiegend

Achtung: fettleibige Mäuse haben einen höheren Titer an 'Firmicutes' im Vgl. zu normalgewichtigen. Dort sind die 'Bacteriodetes' überwiegend

Firmicutes (Clostridien, Bacilli und einige andere Gram-positive) produzieren viel Acetat und andere kurzkettige C-Säuren ….

…. die wiederum schnell in die Blutbahn abgegeben und in der Leber verstoffwechselt werden (Actetat → → Glykogen, Gluconeogenese) ….

…. und zum Aufbau von Fettgewebe führen ….

Fecal transplants (the power of poop)

Microbial communities

Healthy bacteria

Enterobacteriacae
Enterococcus faecalis
Escherichia coli Nisslestämme 1917

und MSB in diversen Kombinationen
Lactobacillus acidophilus, L. reuteri, L. plantari, L. casei,
L. ramnosus und andere
Bifidobacterium sp.
Streptococcus lactis und Verwandte

Managing the Human Microbiome

Fitness-Pillen aus Darmbakterien